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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,810	01/17/2001	Kjell Olmarker	003300-737	4391

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Benton S. Duffett, Jr.  
BURNS, DOANE, SWECKER, & MATHIS, L.L.P.  
P.O. Box 1404  
Alexandria, VA 22313-1404

EXAMINER

SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
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1647

DATE MAILED: 03/11/2003

19

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/760,810	<b>Applicant(s)</b> OLMARKER ET AL.	
	<b>Examiner</b> Jegatheesan Seharaseyon	<b>Art Unit</b> 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) See Continuation Sheet is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-3,5-7,9-11,13-15,17-19,21-23,25,26,28-30,32-34,36-38,40-42,44-46 and 48 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☒ All   b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____.  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____. | 6) <input type="checkbox"/> Other: _____                                    |

### **DETAILED ACTION**

1. The FINALITY of the Office action mailed on 9/9/02 (Paper No: 17) has been withdrawn in order to continue persecution on the merits of this case. The indicated allowability of claims 1-3, 5-7, 9-11, 13-15, 17-19, 21-23, 25, 26, 28-30, 32-34, 36-38, 40-42, 44-46 and 48 in the Office action mailed 9/9/02 has been withdrawn so that previous rejections made in the Office action mailed 5/21/02 (Paper No: 13) from issue so that the previous rejections over art can be maintained and new grounds of rejection over the art can be made. This Office action is in response to the amendment and reply filed on 8/30/02 in Paper No: 15. Thus, claims 1-3, 5-7, 9-11, 13-15, 17-19, 21-23, 25, 26, 28-30, 32-34, 36-38, 40-42, 44-46 and 48 are pending and persecution on the merits continues.
2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.
3. Applicants' changing of the title is acknowledged.

#### ***Claim Rejections - 35 USC § 112, second paragraph withdrawn***

4. Applicants' amendment and arguments have obviated the rejection of claims 27, 28, 31, 32, 35, 36, 39, 40, 43, 44, 47 and 48 under U.S.C § 112, second paragraph, as failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

#### ***Claim Rejections - 35 USC § 101 withdrawn***

5. Applicants' amendment and canceling of claims 27, 31, 35, 39, 43 and 47 have obviated the rejection of claims 27, 28, 31, 32, 35, 36, 39, 40, 43, 44, 47 and 48 under

U.S.C § 101, because the claimed recitation of a use, without setting forth any steps involved in the process.

***Claim Rejections - 35 USC § 112, first paragraph withdrawn***

6. Applicants amendments have obviated the rejection of claims 1-48, rejected under 35 USC 112, first paragraph, for lack of written description and for the scope of enablement.

***Claim Rejections - 35 USC § 102(a), maintained***

7. The rejection of claim 1 under 35 U.S.C. 102(a) as being anticipated by Sommer et al. (1997) is reinstated as presented in Paper NO: 13 mailed on 5/21/02. Although Applicant has amended the claim to recite that the nerve disorder is mediated by nucleus pulposus, the method of treatment is inherently the same as that described in the art. The prior art recognizes that the damage to nucleus pulposus results in nerve disorders associated with nerve root injury as evidenced by Olmarker et al. (Spine, Vol.19, No: 16, pp1803-1808). Olmarker et al. also suggests that inflammatory mechanisms to be of pathogenetic significance in disc herniation with sciatica. Applicant's apparent elucidation of an underlying mechanism or mode of action for known compounds does not make the method of treatment using the same, patentably distinct. Sommer et al. also discusses the using of drugs that reduce the level of functionally active TNF- $\alpha$  in serum in painful inflammatory diseases including rheumatoid arthritis (page: 45, 1<sup>st</sup> paragraph). Claims 1-3, 5-7, 9-11, 13-15, 17-19, 21-23, 25, 28, 32, 36, 44, and 48 are rejected insofar it depends on rejected claim 1.

***Claim Rejections - 35 USC § 103(a), maintained***

8. The rejection of claims 2-3, 5-7, 9-11, 13-15, 17-19, 21-23, 25, 26, 28-30, 32-34, 36-38, 40-42, 44-46 and 48 under 35 U.S.C. 103(a) as being unpatentable over Sommer et al. (1997) in view of Xue et al. (U. S. Patent No. 5,703,092) is reinstated for the reasons stated above in paragraph 7, and Paper No: 13 mailed 5/21/02. In addition, Applicant asserts that the Xue et al. reference does not teach that inhibiting TNF- $\alpha$  will treat nerve disorders. However, the teachings of treating nerve disorders by inhibiting TNF- $\alpha$  by metalloproteinase inhibitor, was provided by Sommer et al. reference. Xue et al. reference was primarily included to teach the various methods of administration etc. (see page: 9, 2<sup>nd</sup> paragraph of Paper No: 13). Furthermore, inhibiting the functionally active TNF- $\alpha$  in the treatment of nerve disorders or immune diseases was recognized in the prior art and Sommer et al. Thus, one skilled in the art would have been motivated to modify the methods disclosed in Sommer et al. using the teachings of Xue et al. to treat nerve disorders by using metalloproteinase inhibitor to inhibit TNF- $\alpha$ . Therefore, the instant invention is obvious over Sommer et al. (1997) in view of Xue et al. (U. S. Patent No. 5,703,092).

***Claim Rejections - 35 USC § 103(a), withdrawn***

9. The rejection of claims 1-3, 5-7, 9-11, 13-15, 17-19, 21-23, 25, 26, 28-30, 32-34, 36-38, 40-42, 44-46 and 48 under 35 U.S.C. 103(a) as being unpatentable over Wang et al. (1996) in view of Xue et al. (U. S. Patent No. 5,703,092) is withdrawn, because of Applicants' persuasive arguments against the teaching of Wang et al.

10. New grounds of rejections.

***New Claim Rejections - 35 USC § 103(a)***

Art Unit: 1647

11. Claims 2-3, 5-7, 9-11, 13-15, 17-19, 21-23, 25, 26, 28-30, 32-34, 36-38, 40-42, 44-46 and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sommer et al. (1997) in view of Amin et al., U.S. Patent No. 6,319,910, effective filing date Dec. 19, 1997.

The instant invention is directed to treatment of a nerve disorder mediated by nucleus pulposus in a mammal by inhibiting TNF- $\alpha$  by administering of metalloproteinase inhibitor (TNF- $\alpha$  inhibitor).

The relevance of Sommer et al. has been set forth above. However, Sommer et al. do not explicitly recite the administration of TNF- $\alpha$  inhibitor containing pharmaceutical to a human. They also do not disclose the administration of the inhibitor systemically, orally or intramuscularly.

Amin et al. teach that chemically modified tetracyclines, including doxycycline, are a class of non-steroidal anti-inflammatory drugs which inhibit TNF- $\alpha$ , and can be used for treating diseases or disorders associated with elevated activities of TNF- $\alpha$  (see abstract, column 3, line 55- column 4, line 2). Amin et al. also teach an effective amount of a chemically modified tetracycline used in a method for treating a disease or disorder associated with elevated levels of TNF- $\alpha$ , including neurodegenerative disorders (column 5, line 65 to column 6, line 24), that the invention is particularly useful in the treatment of humans, that the active principal may be administered by any means that achieves its intended purpose such as parenteral routes, subcutaneous, intravenous, intradermal, intramuscular, orally and other routes, and that the dosage administered will be dependent upon the age, sex, health and weight of the recipient,

kind of concurrent treatment, frequency of treatment and nature of the effect desired, and that the most preferred dosage will be tailored to the individual subject, as is understood and determinable by one of skill in the art (column 6, line 41 to column 7, line 13).

It would have been *prima facie* obvious to the person of ordinary skill in the art at the time the invention was made to use the methods disclosed in Sommer et al. to treat neurological conditions by administering TNF- $\alpha$  inhibitor containing pharmaceutical composition to a human as described in Amin et al. Since Sommer et al. teach that in experimental neuropathies results in increased levels of TNF- $\alpha$ , which can be reduced by TNF- $\alpha$  inhibitors, and since many nerve disorders such as spinal cord injury result in inflammation and increase in TNF- $\alpha$ , the skilled artisan would be motivated to treat any of these nerve disorders/injuries with the methods of Amin et al. Although nucleus pulposus-induced nerve injury may not have been disclosed in the prior art, the method of treatment using TNF- $\alpha$  inhibitors is the same. Elucidation of an underlying mechanism does not make the method of treatment patently distinct. There would be a reasonable expectation of success, since TNF- $\alpha$  inhibitors have successfully been used to treat a large number of disorders that are associated with an increased TNF- $\alpha$ . Therefore, the instant invention is obvious over Sommer et al. (1997) in view of Amin et al. (U. S. Patent No. 6,319,910).

12. No claim is allowed.

### Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

*Gary A. Kunz*  
GARY KUNZ  
SUPERVISOR, PATENT EXAMINER  
TECHNICAL CENTER

JS  
March 7, 2003